

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

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Washington, DC 20231  
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

<b>Date of mailing (day/month/year)</b> 08 June 1999 (08.06.99)	
<b>International application No.</b> PCT/AU98/00919	<b>Applicant's or agent's file reference</b> CAINE
<b>International filing date (day/month/year)</b> 05 November 1998 (05.11.98)	<b>Priority date (day/month/year)</b> 05 November 1997 (05.11.97)
<b>Applicant</b> LOUIS, William, J. et al	

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

12 May 1999 (12.05.99)



in a notice effecting later election filed with the International Bureau on:

2. The election



was



was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO  
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1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

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Datum/Date

14.08.2001

Zeichen/Ref./Réf. <b>HMJ03328EP</b>	Anmeldung Nr./Application No./Demande n°//Patent Nr./Patent No./Brevet n° <b>98952426.9-2101/AU9800919</b>
Anmelder/Applicant/Demandeur//Patentinhaber/Proprietor/Titulaire <b>THE UNIVERSITY OF MELBOURNE</b>	

## COMMUNICATION

The European Patent Office herewith transmits the partial European search report under Rule 46(1) EPC relating to the above-mentioned European patent application.

Copies of the documents cited in the search report are enclosed.

The applicant's attention is drawn to the following:

The search Division informs the applicant that if the European search report is also to cover inventions other than the invention first mentioned in the claims, a further search fee must be paid for each of these inventions, within ONE MONTH after notification of this communication.

If the application has been filed up to 30 June 1999, the search fee in force before 01 July 1999 (EUR 869,--) or the equivalent applicable on the date of payment is payable.

**This applies also to the search fees requested under Rule 46(1) EPC.**

See also OJ EPO 06/1999, 405.

Moreover, the Search Division considers that the present European patent application does not comply with the provisions of the European Patent Convention to such an extent that it is not possible to carry out a meaningful search into the state of the art on the basis of some of the claims; reference is made to sheet C, which is attached to the search report.

- ☐ The abstract was modified by the Search Division and the definitive text is attached to the present communication.
- ☒ Additional set(s) of copies of the documents cited in the European search report is (are) attached as well.

### Note to users of the automatic debiting procedure:

Unless the EPO receives prior instructions to the contrary, the search fee(s) will be debited on the last day of the period for payment. For further details see the Arrangements for the automatic debiting procedure, Supplement to OJ EPO 02/1999.



REGISTERED LETTER



European Patent  
Office

**SUPPLEMENTARY  
PARTIAL EUROPEAN SEARCH REPORT**

Application Number

under Rule 46, paragraph 1 of the European Patent Convention EP 98 95 2426

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
A	P TIMMERMANS: "Quantitative relationship between alpha-adrenergic activity and binding affinity of alpha-adrenoceptor agonists and antagonists" J MED CHEM, vol. 27, 1984, pages 495-503, XP001008253 see compound 35 ---	1-29	C07D263/28 C07D263/12 C07D265/08 C07D277/10 C07D277/18 C07D277/60 C07D279/06 C07D279/08 C07K14/705 C07H21/00
A	P TIMMERMANS: "Characterisation of alpha-adrenoceptor populations" J MED CHEM, vol. 24, no. 5, 1981, pages 502-507, XP002911672 * the whole document * ---	1-29	
X	DECKERT V ET AL: "CONTRIBUTION OF ALPHA2-ADRENOCEPTORS TO THE CENTRAL CARDIOVASCULAR EFFECTS OF CLONIDINE AND S 8350 IN ANAESTHETIZED RATS" CLINICAL AND EXPERIMENTAL PHARMACOLOGY AND PHYSIOLOGY, XX, XX, vol. 18, 1991, pages 401-408, XP000985701 see S-8350 --- -/--	1-29	TECHNICAL FIELDS SEARCHED (Int.Cl.6)  C07D A61K
<b>LACK OF UNITY OF INVENTION</b>			
<p>The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:</p> <p>see sheet B</p> <p>The present partial European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims.</p>			
Place of search <b>MUNICH</b>		Date of completion of the search <b>25 July 2001</b>	Examiner <b>Scruton-Evans, I</b>
<b>CATEGORY OF CITED DOCUMENTS</b> X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons ..... & : member of the same patent family, corresponding document	

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EPO FORM 1503 03.82 (P4/C23)



DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
X	WO 95 11021 A (ALLERGAN INC) 27 April 1995 (1995-04-27) * the whole document *	1-29	
X	HIRASHIMA A ET AL: "SYNTHESIS AND OCTOPAMINERGIC-AGONIST ACTIVITY OF 2-(ARYLAMINO)OXAZOLIDINES AND 2-(SUBSTITUTED BENZYLAMINO)-2-OXAZOLINES" JOURNAL OF PEPTIDE SCIENCE, JOHN WILEY AND SONS LTD, GB, vol. 21, 1996, pages 419-424, XP000985703 ISSN: 1075-2617 * the whole document *	1-29	
			TECHNICAL FIELDS SEARCHED (Int.Cl.6)



The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. Claims: 1-29

Compounds of the formula II (and the dependent formulae thereof), and their pharmaceutical use and compositions thereof

2. Claims: 30-37

An isolated Ox receptor, an isolated nucleic acid molecule that encodes such an Ox receptor, and a recombinant molecule comprising such a nucleic acid molecule, together with a method of identifying a modulator of Ox receptor activity.

The claims 1-29 are concerned with compounds of a defined structure which have an associated activity, namely an Ox receptor activity, and attempt to provide a solution to the problem of providing novel compounds with this activity. The "special technical feature" of this invention is the formula II (and the dependent formulae)

Claims 30-35 are concerned with an Ox receptor per se (albeit without any defining features), a nucleic acid molecule that encodes this Ox receptor, and a recombinant molecule comprising such a nucleic acid molecule. The receptor bears no technical relationship to the structure of the compounds, and provides a solution to the problem of isolating the specific receptor associated with an activity. There is no single general inventive concept linking this subject matter with that of claims 1-29, and consequently there is a lack of unity a priori.

Claims 36-37 define a method for identifying a modulator of Ox receptor activity, the modulator being undefined, and unrelated to the compounds of claim 1-29, thus not sharing the special technical feature of claims 1-29 and lacking unity a priori with these claims.

The application has been divided into the above (groups of) inventions which individually are considered to meet the requirement of unity. If additional fees are paid for (one or more of) the, as yet, unsearched invention(s), the subsequent search(es) might reveal prior art which leads to a finding of lack of unity a posteriori within (one or more of) the, as yet, unsearched invention(s). Should this be the case, as a rule, no further invitation to pay additional fees will be issued. Only the first identified invention in each group of inventions, for which additional search fees have been paid in due time and which subsequently is considered to lack unity, will be searched.



Claim(s) searched completely:  
8-16

Claim(s) searched incompletely:  
1-7, 17-29

Reason for the limitation of the search:

Present claims 1-20<sup>29?</sup> relate to a compound defined by reference to a desirable characteristic or property, namely that it have a selectivity for an O<sub>x</sub> receptor over one or both of the alpha-2 or I<sub>2</sub>-receptors of greater than 1. The claims cover all products having this characteristic or property, whereas the application provides support within the meaning of Article 84 EPC and/or disclosure within the meaning of Article 83 EPC for only a very limited number of such products. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 84 EPC). An attempt is made to define the product by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds of claims 8-16, independent of their functional definition given in claim 1.

EP 98 95 2426

25-07-2001

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9511021 A	27-04-1995	US 5580892 A	03-12-1996
		AU 678641 B	05-06-1997
		AU 8122694 A	08-05-1995
		CA 2174544 A	27-04-1995
		EP 0724439 A	07-08-1996
		JP 9506339 T	24-06-1997
		US 5708015 A	13-01-1998

REC'D 15 NOV 1999

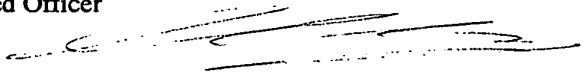
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PCT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 2122936/MJC/RR	<b>FOR FURTHER ACTION</b>	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International application No. <b>PCT/AU 98/00919</b>	International filing date ( <i>day/month/year</i> ) 5 November 1998	Priority Date ( <i>day/month/year</i> ) 5 November 1997
International Patent Classification (IPC) or national classification and IPC  <b>Int. Cl.<sup>6</sup></b> C07D 263/28, 263/12, 265/08, 277/10, 277/18, 277/60, 279/06, 279/08, C07K 14/705, C07H 21/00, G01N 33/566, A61K 31/42		
Applicant <b>THE UNIVERSITY OF MELBOURNE et al.</b>		

1.	This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2.	This REPORT consists of a total of 4 sheets, including this cover sheet.  <input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).  These annexes consist of a total of 14 sheet(s).
3.	This report contains indications relating to the following items:
I	<input checked="" type="checkbox"/> Basis of the report
II	<input type="checkbox"/> Priority
III	<input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	<input type="checkbox"/> Lack of unity of invention
V	<input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	<input type="checkbox"/> Certain documents cited
VII	<input type="checkbox"/> Certain defects in the international application
VIII	<input type="checkbox"/> Certain observations on the international application

Date of submission of the demand 12 May 1999	Date of completion of the report 4 November 1999
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200 WODEN ACT 2606 AUSTRALIA Facsimile No. (02) 6285 3929	Authorized Officer   <b>CHRISTINE BREMERS</b> Telephone No. (02) 6283 2313



**I. Basis of the report**1. With regard to the **elements** of the international application:\*☐ the international application as originally filed.☒ the description, pages **1-3, 6-48** , as originally filed,

pages , filed with the demand,

pages **4,5** , filed with the letter of **22 October 1999** .☒ the claims, pages , as originally filed,

pages , as amended (together with any statement) under Article 19,

pages , filed with the demand,

pages **49-50, 52-54, 56-57 and 60** , filed with the letter of **10 September 1999**pages **51, 55, 58 and 59**, filed with the letter of **22 October 1999**.☐ the drawings, pages , as originally filed,

pages , filed with the demand,

pages , filed with the letter of .

☐ the sequence listing part of the description:

pages , as originally filed

pages , filed with the demand

pages , filed with the letter of .

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).☐ the language of publication of the international application (under Rule 48.3(b)).☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, was on the basis of the sequence listing:☐ contained in the international application in written form.☐ filed together with the international application in computer readable form.☐ furnished subsequently to this Authority in written form.☐ furnished subsequently to this Authority in computer readable form.☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished4. ☐ The amendments have resulted in the cancellation of:☐ the description, pages☐ the claims, Nos.☐ the drawings, sheets/fig.5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be nonobvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos.: **1-44 in part**

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claim Nos. **1-10 (report based on search on "Oxazoline receptor" and "Rilmenide receptor" as no sequence or structure given); Claims nos. 11-44 (report based on search of examples).**

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. Statement**

Novelty (N)	Claims 1-44	YES
	Claims	NO
Inventive step (IS)	Claims 1-44	YES
	Claims	NO
Industrial applicability (IA)	Claims 1-44	YES
	Claims	NO

**2. Citations and explanations (Rule 70.7)**

1. Chemical Abstracts, vol. 126, Abs. No. 28014
2. Chemical Abstracts, vol. 115, Abs. No. 174324
3. Chemical Abstracts, vol. 109, Abs. No. 2427
4. Chemical Abstracts, vol. 94, Abs. No. 30739
5. Chemical Abstracts, vol. 95, Abs. No. 12764
6. Chemical Abstracts, vol. 88, Abs. No. 136337
7. Chemical Abstracts, vol. 88, Abs. No. 121228
8. Chemical Abstracts, vol. 85, Abs. No. 5611
9. US 3988464
10. US 5034406
11. US 3598833
12. US 4102890
13. US 4378366
14. AU 75331/94
15. US 4267345
16. European Journal of Pharmacology
17. Annals of the New York Academy of Sciences

**NOVELTY (N) and INVENTIVE STEP(S)**

1. None of documents 1-17 disclose an oxazoline receptor or compounds of formula I as modulators of Ox receptor activity.

Therefore claims 1-10 are considered novel and inventive.

2. None of documents 1-17 disclose the compounds of formula II as per claims 11-36 or their use as per claims 37-44.

Further, the present compounds of formulas I and II are said to have the inherent property of having a selectivity for an Ox receptor, over one or both of the  $\alpha_2 I_1$ - and  $I_2$ -receptors, of greater than 1. There is no disclosure in any of documents 1-17 that the compounds of the present invention would have this inherent property or that they would bind to or be an agonist/antagonist for an Ox receptor.

Thus claims 11-44 are novel and inventive in light of documents 1-17.



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>6</sup> :</b> <b>C07D 263/28, 263/12, 265/08, 277/10, 277/18, 277/60, 279/06, 279/08, C07K 14/705, C07H 21/00, G01N 33/566, A61K 31/42</b>	<b>A1</b>	<b>(11) International Publication Number:</b> <b>WO 99/24411</b> <b>(43) International Publication Date:</b> 20 May 1999 (20.05.99)
<b>(21) International Application Number:</b> PCT/AU98/00919 <b>(22) International Filing Date:</b> 5 November 1998 (05.11.98) <b>(30) Priority Data:</b> PP 0202 5 November 1997 (05.11.97) AU <b>(71) Applicant (for all designated States except US):</b> THE UNIVERSITY OF MELBOURNE [AU/AU]; Grattan Street, Parkville, VIC 3052 (AU). <b>(72) Inventors; and</b> <b>(75) Inventors/Applicants (for US only):</b> LOUIS, William, J. [AU/AU]; P.O. Box 21, Rosanna, VIC 3084 (AU). JACKMAN, Graham, P. [AU/AU]; 152 Ferntree Gully Road, North Clayton, VIC 3168 (AU). CONWAY, Elizabeth, L. [AU/AU]; 11 Goodall Street, Hawthorn, VIC 3122 (AU). GUNDLACH, Andrew, L. [AU/AU]; 546 Barkers Road, Hawthorn East, VIC 2123 (AU). IAKOVIDIS, Dimitri [AU/AU]; 183 Church Road, Doncaster, VIC 3108 (AU). KING, Paul, R. [AU/AU]; 6 Mitchell Street, Brunswick, VIC 3056 (AU). LOUIS, Simon, N., S. [AU/AU]; 46 Fergie Street, North Fitzroy, VIC 3068 (AU). NERO, Tracy [AU/AU]; 42 Oberon Avenue, St. Albans, VIC 3021 (AU).	<b>(74) Agents:</b> SLATTERY, John, M. et al.; Davies Collison Cave, 1 Little Collins Street, Melbourne, VIC 3000 (AU). <b>(81) Designated States:</b> AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). <b>Published</b> <i>With international search report.</i>	
<b>(54) Title:</b> RECEPTOR WITH AN AFFINITY FOR COMPOUNDS OF THE OXAZOLINE CLASS <b>(57) Abstract</b> <p>The present invention relates to a novel receptor, in particular to a new type of receptor with an affinity for compounds of the oxazoline class, compounds which bind to this receptor, and the use of these compounds in the treatment of diseases, especially diseases of the central nervous system, the cardiovascular system and the kidney.</p>		

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